

Remarks

Claims 1-22 are pending in the instant application. The specification is objected to for lacking cross-reference to priority information, headings for each section thereof, and an abstract. Claims 21-22 stand rejected under 35 U.S.C. §101. Claims 1-22 stand rejected under 35 U.S.C. §112, second paragraph. Specifically, claims 1, 2, 5, 11, 12, and 21-22 are objected to. Claims 1-22 are rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of United States Patent No. 6,375,931. Claims 1-13, 15-19, 21-22 stand rejected under 35 U.S.C. §102(e) as being anticipated by United States Patent No. 5,846,517 to Unger (Unger I). Claims 1-12, 15-18, 21-22 stand rejected under 35 U.S.C. §102(e) as being anticipated by United States Patent No. 5,733,572 to Unger (Unger II). Claims 1-22 stand rejected under 35 U.S.C. §102(e) as being anticipated by United States Patent No. 6,375,931 to Ostensen. Claims 1-22 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Unger II. The specification has been amended. The claims have been amended. Claims 2, 11, and 12 have been amended. Claims 21 and 22 have been cancelled without prejudice. New claims 23 and 24 have been added. Applicants respectfully submit that none of the amendments constitute new matter in contravention of 35 U.S.C. §132. Reconsideration is respectfully requested.

Applicants acknowledge the maintenance of the Restriction Requirement and the election of species and their respective subgenus of phospholipids and alkylsulphates.

The specification is objected to for lacking cross-reference to priority information, headings for each section thereof, and an abstract. These objections have been obviated by the insertion of the missing cross-references and headings for each section of the specification. An abstract is also submitted on a separate sheet. Reconsideration and withdrawal of the objections is respectfully requested.

Claims 21-22 stand rejected under 35 U.S.C. §101 as being an improper definition of a process. This rejection has been obviated by the cancelling, without prejudice, of claims 21 and 22. Reconsideration and withdrawal of the rejections are respectfully requested.

Claims 1-22 stand rejected under 35 U.S.C. §112, second paragraph. Specifically, claims 1, 2, 5, 11, 12, and 21-22 are objected to. These objections are respectfully obviated or traversed.

Claim 1 is objected to for reciting “a combined presentation”. Claim 1 has been corrected to recite “a combined preparation”.

Claim 2 is objected to for being ambiguous. Claim 2 has been amended to more distinctly claim the present invention. Specifically, claim 2 has been amended to recite a list of possible candidates that make up the dispersed gas. The list also includes any mixture formed from the listed candidates.

Claim 5 is objected to for reciting “an initially coalescence-resisting surface membrane,...”. This objection is respectfully traversed. The instant application defines this term by reference to WO-A-8002365 and provides gelatin as an example. Reconsideration and withdrawal of the rejection are respectfully requested.

The Applicant has been encouraged to employ formal Markush language in claims 11 and 12. Claims 11 and 12 have been amended to incorporate the language recommended by the Examiner.

Claims 21-22 are rejected for not reciting active, positive steps. This rejection is obviated by the cancellation of claims 21 and 22 from the instant application. Reconsideration and withdrawal of the rejection are respectfully requested.

Applicants respectfully submit that each of the Examiner’s rejections under 35 U.S.C. §112 have been either obviated by amendment or traversed. Reconsideration and withdrawal of these rejections is respectfully requested.

Claims 1-22 are rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of United States Patent No. 6,375,931. This rejection is respectfully traversed.

The present invention is directed to a combination of injectable aqueous gas dispersions and separately administrable destabilising substances.

Applicants respectfully submit that the present invention, as claimed in claim 1, is unambiguously different from the invention claimed in US 6,375,931, where substances such as electrolytes, sugars, polyols, oils and polyethylene glycol are disclosed as integral constituents of gas microbubble dispersions. There is no suggestion in US 6,375,931 that such materials can be co-administered as a separate component in order to promote microbubble growth by destabilising the microbubble dispersion.

As the '931 patent fails to disclose, teach, or suggest the co-administration of the combination as claimed, Applicants respectfully submit that the claims of the present invention are patentably distinct from the claims of the '931 patent. Reconsideration and withdrawal of the double patenting rejection are respectfully requested.

Claims 1-13, 15-19, 21-22 stand rejected under 35 U.S.C. §102(e) as being anticipated by United States Patent No. 5,846,517 to Unger (Unger I). This rejection is respectfully traversed.

Unger I discloses use of an intermittent imaging technique in which ultrasonication is suspended while injected microbubbles perfuse an organ of interest and undergo some increase in size in the absence of compressive effects generated by ultrasound irradiation. The resumption of ultrasonication is said to produce an improved signal, since backscatter increases with the sixth power of the radius of the expanded microbubbles. The Examiner further states that Unger I discloses coadministration of

compositions comprising gaseous liposomes dispersions and a vasodilator such as enalapril.

Unger I, however, fails to disclose the administration of destabilising substances to promote controlled growth of microbubbles to effect their temporary retention in the tissue microvasculature as is claimed by the present invention. Applicants submit that Unger I uses a vasodilator in order to dilate the vasculature of the renal region. While Applicants also disclose and claim the use of vasodilator in a dependent claim, the vasodilator only is employed to affect the size of the vasculature, not the size of the dispersed gas. Therefore, as Unger I fails to disclose coadministration of a substance or substances capable of destabilising the dispersed gas so as to at least transiently increase the size thereof, Unger fails to disclose each and every element of the present invention. Accordingly, Applicants respectfully submit that Unger I does not anticipate the present invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-22 stand rejected under 35 U.S.C. §102(e) as being anticipated by United States Patent No. 6,375,931 to Ostensen. This rejection is respectfully traversed.

As noted hereinabove, Ostensen fails to disclose, teach, or suggest that the substances which affect the size of the dispersed gas may be separately administered. The Ostensen substances such as electrolytes, sugars, polyols, oils and polyethylene glycol are disclosed as being integral constituents of gas microbubble dispersions themselves. The present invention, on the other hand, distinctly claims that such

materials are co-administered as a separate component in order to promote microbubble growth by destabilising the microbubble dispersion.

Applicants respectfully submit that as Ostensen fails to disclose, teach, or suggest the co-administration of the separate components as claimed, Ostensen fails to disclose each and every element of the present invention so that the present invention is patentably distinguishable thereover. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-12, 15-18, 21-22 stand rejected under 35 U.S.C. §102(e) as being anticipated by United States Patent No. 5,733,572 to Unger (Unger II). This rejection is respectfully traversed.

Unger II is related to topical and subcutaneous delivery vehicles for various active ingredients, such as drugs and cosmetics. The microspheres disclosed in Unger II are adapted for this purpose, and not for use as an ultrasound contrast agent as is claimed by the present invention.

Applicants respectfully submit that Unger II fails to disclose each and every limitation of the present invention. Unger II provides no disclosure, and the Examiner cites no teachings therein, of a contrast agent preparation of a combination of injectable aqueous gas dispersions and separately administrable destabilising substances which are capable of increasing the size thereof. Therefore, as Unger II fails to disclose each and

every element of the claimed invention, Applicants respectfully submit that the present invention is novel thereover. Reconsideration and withdrawal of the rejection are respectfully requested.

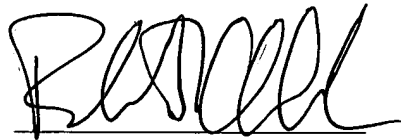
Furthermore, Claims 1-22 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Unger II. This rejection is respectfully traversed.

Applicants respectfully submit that Unger II fails to disclose, teach, or suggest the present invention. The Examiner's rejection is based on particular materials used by Unger and on the purported obviousness of using these materials with adenosine as a vasodilator. However, Applicants again respectfully submit that Unger II does not disclose, teach, or suggest a separately administrable substance or substances capable of destabilising the dispersed gas so as to increase the size thereof for use as a contrast agent. The use of the Unger II materials with adenosine as a vasodilator does not correct this deficiency in Unger II. As noted above, the vasodilator affects the vasculature, not the size of the dispersed gas. Therefore, the combination of Unger II with adenosine thus does not establish a prima facie case that the present invention is obvious. As the combination of Unger II with adenosine fails to disclose, teach, or suggest the claims of the present invention, Applicants respectfully submit that the present invention is patentably distinct thereover. Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the amendments and arguments hereinabove, Applicants respectfully submit that the instant application, including claims 1-20 and 23-24, is in condition for allowance. Favorable action thereon is respectfully requested.

Any questions with respect to the foregoing may be directed to Applicants's undersigned counsel at the telephone number below.

Respectfully submitted,



Robert F. Chisholm
Registration No.: 39,939
Attorney for Applicants

Amersham Biosciences Corp
800 Centennial Avenue
P. O. Box 1327
Piscataway, New Jersey 08855-1327

Tel: (609) 514-6905
Fax: (609) 514-6635

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Melissa Leck
Signature [Signature]
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